be due to exposure; he or she should see a supervised worker who has been absent from work more than two weeks owing to illness. These absences should be reviewed on a group and individual basis. If indicated, medical examination should be undertaken at any time. Section 16 provides for the keeping of confidential medical records of all supervised workers; these must not be destroyed without the agreement of the Chief Employment Medical Adviser.

The purpose of the present symposium is to review British experience of the environmental, clinical, epidemiological and pathological effects of exposure to vinyl chloride arising in the course of polymerization of vinyl chloride monomer to polyvinyl chloride, and to exchange information.

The implications of the association of angiosarcoma of the liver with exposure of workers to vinyl chloride monomer have had such a profound effect on industry, workers and governments that these effects must be seen in the wider context of occupational carcinogenesis generally. I think it is necessary to consider what the future may hold in the way of carcinogenic risks. We can, I believe, regard the experience we have gained throughout the world with vinyl chloride as a pilot study on a newly discovered occupational carcinogen. Frank and open discussion between government departments and both sides of industry is indispensable to the achievement of success.

Postscript

The Working Group on Vinyl Chloride Code of Practice for Health Precautions met on 8 October 1975 and adopted a new hygiene standard agreed by the Working Group as 'a ceiling value of 30 ppm and a time weighted average of 10 ppm, allowing that wherever practicable exposure should be brought as near as possible to zero concentrations.' The figures of 30 parts/10^6 and 10 parts/10^6 replace the original figures of 50 parts/10^6 and 25 parts/10^6.

Other requirements of the Code, including medical supervision, are currently being reviewed.

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Vinyl Chloride and the Production of PVC

Polymerization Characteristics of Vinyl Chloride

Vinyl chloride has a boiling point of −13.5°C: under normal pressures and temperatures it is a gas. In its liquefied form under pressure, it can be readily polymerized at temperatures in the range 40–70°C to give polyvinyl chloride (PVC), a white solid material. The addition polymerization of about 500–1500 molecules of vinyl chloride produces one molecule of PVC and the polymerization reaction is strongly exothermic. The polymer itself is insoluble in the liquid monomer and so precipitates out as it is produced. The polymer is, however, capable of absorbing high proportions of monomer (40% by weight) so that as the polymerization reaction proceeds and more polymer is precipitated, so equally is more monomer absorbed by the polymer to the point at about 70% conversion where monomer as a separate liquid phase disappears and the remaining monomer must be polymerized in its dissolved state within the swollen polymer. As this phase of the polymerization proceeds, the concentration of monomer in the polymer decreases and the rate of reaction correspondingly diminishes until at about 92–95% total conversion the speed of polymerization becomes uneconomically slow. These are the fundamental characteristics of vinyl chloride and its polymerization mechanism which decide the principal features of industrial processes for the production of PVC.

The Production Process for PVC
Because it must be polymerized in liquefied form at temperatures above its boiling point, the industrial process must be carried out in pressure vessels (at 50°C the vapour pressure of vinyl chloride is ~7 atmospheres). Because the reaction is exothermic, means must be found for removal of the heat produced so that the temperature of reaction (and thus the pressure, and the properties of the end-product) may be kept under control. In the most widely used process, this control is achieved by dispersing the liquid monomer into tiny droplets (about 100 μm in diameter) in approximately equal quantities of water, by means of mechanical agitation together with the addition of small quantities of surface-active agents which facilitate the breakdown of the monomer into droplets and stabilize it in this form. This fine subdivision of liquid monomer enables the heat evolved from the polymerizing monomer to be rapidly transferred to the surrounding water and then removed by a cooling jacket on the reactor, the process being aided by agitation. The subdivision of the monomer into droplets has also the vital property of ensuring that the polymer, which is produced within each droplet, is presented at the end of the reaction in finely divided, powder form, and not as an intractable horny mass.

As polymerization proceeds, the two phase system of monomer dispersed in water becomes a three phase system of solid polymer precipitated within liquid monomer droplets which are in turn dispersed in a continuous water phase. A great deal of research has been devoted in the past thirty years to the control and stabilization of this rather delicate colloidal system but, even so, small quantities of polymer are still thrown out from it and form a thin continuous film of PVC on the walls of the reactor. If left, this will increase in thickness and, since PVC is a poor thermal conductor, will reduce the heat transfer characteristics of the vessel and make temperature control impossible. At the end of the reaction it is therefore essential that this film should be cleaned away. This is one of the basic reasons why a truly continuous process has never yet been developed for making PVC and why the polymer, the world over, is still made by a batch process in relatively small reactors. This, as we shall see, has a significant influence on the ease of controlling fugitive monomer in a PVC plant.

As polymerization nears 90–92% conversion, the rate of reaction slows down markedly and at about 95% conversion has become so slow as to be quite uneconomic. There is no possibility therefore of continuing polymerization to 100% conversion and solving some of the problems connected with vinyl chloride toxicity in this way. At the termination point of the reaction, therefore, the 5–6% residual monomer (still at a pressure of 4–5 atmospheres) is vented back to a gasholder and a slurry of PVC particles (100–150 μm diameter), suspended by stirring in water, is left in the reactor.

Now to a description of the process in engineering rather than chemical terms: polymerization is carried out in cylindrical, stirred, jacketed pressure vessels. To begin, water, surfactive agents and free radical catalyst are added to the reactor: the air space above this liquid phase is purged of oxygen (which inhibits polymerization) and liquid vinyl chloride is then injected into the reactor. (In the UK, reactor sizes range from $10m^3$ to $40m^3$ and the monomer charge per batch ranges up to about 15 tons.) The reactor contents are then heated to and maintained at reaction temperature. After a reaction time of the order of eight hours, excess monomer is vented to a gasholder (for recycling) and the reactor is evacuated, at elevated temperature, to strip as much monomer as possible from the polymer on which it is absorbed. The polymer slurry is then transferred to closed tanks prior to the next stage in the process.

Meanwhile the empty autoclave, which still contains vinyl chloride gas at a low partial pressure is further evacuated before opening to atmosphere, and automatic high pressure water cleaning jets are activated to remove polymer scale from the walls. At this stage, the cycle is complete.

Vinyl chloride monomer has a strong affinity for PVC and the last traces of it are difficult to remove from the polymer; the polymer in the slurry after stripping therefore still contains around 500 parts/10^6 of vinyl chloride. This slurry is centrifuged to remove the water phase and the wet powder is then dried in continuous driers; during this process further vinyl chloride is removed in the drier gases and the final dried powder currently contains about 50 parts/10^6 of monomer.

Interfaces between Vinyl Chloride and People
This description of the production process gives some indication of the relative potentials of different parts of the process for creating significant exposures of people to vinyl chloride. If we take a plant capable of making 100 000 tons per annum (tpa) of PVC then the polymerization building will, during the course of a year, have handled over 100 000 tons of vinyl chloride in

liquefied form under pressure. Into the drying section will have passed 50 tons of vinyl chloride in a form strongly absorbed on the polymer and at a concentration on polymer of about 0.05%. In the finished product, 5 tons of vinyl chloride will leave the factory, each year, still absorbed on the polymer at a concentration of 0.005%. Although strictly outside the scope of this paper it is worth proceeding further and pointing out that in further fabrication operations on the polymer, some of this small residual concentration of monomer is driven off so that in the final fabricated article only ~5 parts/10^6 of monomer remain or 0.5 tons out of the original annual total of 100 000 tons. In fabricated articles which are used for foodstuffs packaging (bottles, film and foil), and which represent about 10% of total UK production, the monomer concentration is still lower, and the pro rata amount absorbed on foodstuff containers from a 100 000 tpa plant would be 50 lb. Of this quantity 3½ lb might migrate into the foodstuff where its average concentration is unlikely to exceed 10 parts per thousand million. Since total UK production is about 400 000 tpa this means that the annual ingestion by the average UK citizen cannot exceed 0.0001 g, a figure which agrees well with calculations based on diet analysis.

A final potential interface arises because at points in the production process, vinyl chloride is exhausted to atmosphere. On a typical PVC plant and with current levels of achievement, 0.3% of the monomer is lost to atmosphere: with this performance ground level concentrations at the factory boundary are well below 0.1 parts/10^6 and even these low amounts decay very rapidly with distance. In the band ¼–1 mile (0.4–1.6 km) around one factory, for instance, the concentrations determined are in the range 0.01–0.0001 parts/10^6.

These figures should make clear that by far the biggest potential for exposure exists in the polymerization section of the plant, since here 100 000 tons per year of a liquefied gas under pressure are handled in a confined space, in contrast to other parts of the process and to the later downstream operations of the plastics industry. In these downstream operations the corresponding quantities, this time in the form of absorbed vapour at a low partial pressure and not confined to a single geographic situation, range from 5 tons down to 3 lb per year. That the polymerization section is in fact the area where hazard has existed in the past is confirmed by the fact that all the authenticated cases of vinyl chloride-related angiosarcoma of the liver throughout the world have been of workers engaged in plants where liquid vinyl chloride under pressure was used in large quantities.

The nature of the polymerization process, as described above, illustrates why exposures in the past could have been large. The plants are composed of a large number of batch reactors of small capacity per batch, relative to the total annual throughout. In each reactor, two complete cycles per day are carried out and each cycle requires vinyl chloride to be injected under pressure, heated, contained, stirred and polymerized almost completely: at the end of the cycle unpolymerized monomer has to be removed and the reactor opened and cleaned. The possibilities of small leakages from pumps, valves, stirrer glands and from the opened reactor at the end of the cycle were obviously significant: and the manual cleaning of reactors gave further opportunity for high exposures. This was particularly true during the long period in the 1940s to 1960s when vinyl chloride was thought to be harmless and when a recommended exposure limit did not exist or, late in the 1950s, was set by regulatory authorities, industrial hygienists, &c., at a level of 500 parts/10^6.

The general consensus of opinion throughout the world, today, is that average atmospheric exposure for polymerization workers between 1940 and 1970 might have been of the following orders: 1945–55, ~1000 parts/10^6; 1955–60, ~400–500; 1960–70, ~300–400; mid-1973, ~150; 1975, ~5 parts/10^6. Across the world, there will have been variations around these figures because of differences in plant design or process operation. Even the way in which jobs were organized can have caused variations. In some countries or on some plants workmen were employed specifically to clean out autoclaves (where exposures could have been very high) while in others autoclave cleaning was part only of a whole range of jobs carried out by individual work people. Some spokesmen have suggested, perhaps for full-time cleaners, exposure levels as high as 3000 parts/10^6 in the early days of the industry.

With these very high figures as background, the progress made by the PVC industry in the UK in reducing atmospheric concentrations since the carcinogenic hazard of vinyl chloride became known in early 1974 is shown in Table 1, which also shows improvements made at all the other interfaces described earlier in this paper. Although, as we have seen, the exposure levels in these other places are many orders of magnitude lower than on the polymerization plants, industry has aimed to reduce fugitive vinyl chloride levels at every point in order to eliminate concern wherever it might exist. With work still in progress, all these figures will be reduced further though, in view of the effort already put in, it is likely that the polymerization plant atmospheres are approaching a limiting value of 2–5 parts/10^6.

Table 1

Vinyl chloride monomer levels in UK industry

Polymerization	*January 1974 (parts/10^6)*	*July 1975 (parts/10^6)*
VCM in plant atmosphere (weekly average)	~150	~5
VCM emissions	0.75% of output	0.3% of output
VCM in product	200–500	< 50 for most grades
Fabrication and Use		
VCM in plant atmospheres	2–15	< 2
VCM in PVC bottles	~50	~2
VCM in beverages	0.1	0.01

Finally a few rough calculations of the daily dosages at the current exposure levels and at the higher atmospheric levels which previously could have existed on PVC plants may be helpful in putting current plant performance and present downstream exposures into perspective, one with another, and in comparison with earlier figures (Table 2).

Table 2

Daily dosages at current and earlier exposure levels

	Daily dose (g/kg body weight)
Polymerization plant operator at 1000 parts/10^6	0.36
Polymerization plant operator at 500 parts/10^6	0.18
Polymerization plant operator now at ~5 parts/10^6	0.0018
Fabrication plant operator at 1 part/10^6	0.0004
Average UK citizen through ingestion in food	0.000000004

In later papers to this conference, a wide range of diseases or symptoms which have been associated with or attributed to exposure to vinyl chloride will be discussed. It is important to note that most, if not all, of these have been contracted by people who worked under conditions represented by the highest figures in the above table. Today no one is exposed to doses at this level. The exposure of workers in industry is now at least two orders of magnitude lower, while the general public in the UK absorbs, through foodstuffs, a quantity which is some fifty million times lower.

While the conference will be concentrating primarily on problems which have occurred in the past, I hope it may find some time to consider whether there remains any possibility of similar effects occurring at the markedly lower – and in some areas almost incomprehensibly lower – levels which prevail today. For it is on this, quite properly, that industry, and society generally, have focused their attention in the past eighteen months.

DISCUSSION

Dr M D Kipling (*Employment Medical Advisory Service, Birmingham*) said that it was known that workers bagging the PVC powder were sometimes covered with the dust and that this powder contained a percentage of vinyl chloride monomer. He asked whether any information was available on the particle size of the dust produced in differing processes throughout the world and the incidence of vinyl chloride disease.

Mr A W Barnes replied that the particle sizes of PVC powder did vary very widely, depending on the application for which the PVC powder was made. However, most manufacturers produced all grades of polymer so that it was unlikely that any medical conditions peculiar to a particular manufacturing site could be explained in terms of the polymer and its particle size. Moreover, it should be remembered that all the significant medical effects under discussion at this conference (angiosarcoma, acro-osteolysis &c.) had, throughout the world, been observed exclusively in workers on polymerization plants or, in two cases, plants handling liquid vinyl chloride under pressure. Features common to all these workers were that they were exposed to vinyl chloride vapour in the atmosphere but were not exposed to PVC dust since the polymer was maintained in aqueous suspension throughout this stage of the process.

It was in the drying and bagging sections of the PVC-producing process that exposure to solid PVC particles could arise but, despite extensive medical investigation, no significant abnormalities had been found among drier operators or packers. It was perhaps worth noting, too, that the greater proportion of PVC powder was of a particle size similar to sand so it did not generally pose an airborne dust problem. For those powders which might cause true dust exposures it had been customary in industry, because of the nuisance and discomfort factors alone, to provide some form of respiratory protection.

Dr C S Darke (*Royal Infirmary, Sheffield*) said that he had investigated 14 cases of breathlessness in workers exposed to vinyl chloride monomer. The findings were: no abnormal physical signs; chest radiographs normal; routine respiratory function tests difficult to evaluate but some results slightly below predicted values, especially impaired CO diffusion in 6 individuals; perfusion and ventilation scans showed striking abnormalities as illustrated by one slide revealing marked perfusion defects of upper lobes. One patient underwent open biopsy of each of the three lobes of the right lung. Histology revealed focal alveolar wall thickening with macrophages in the alveolar spaces and increased reticulin and collagen formation seen on electron microscopy. No obvious vascular abnormality except on fluorescent examination. It might be of importance that some of the worst affected men were concerned in a polymerization process that yielded 'plastisol', a very fine PVC powder with particle size around 0.5 μm. These particles, containing vinyl chloride monomer, could be carried to the alveolar walls where they might be retained and thus set up a reaction of the type seen on light microscopy.

Professor I J Selikoff (*Mount Sinai School of Medicine, City University of New York*) said that pulmonary abnormalities had been unexpectedly common findings among some 1200 vinyl chloride polymerization workers in his studies. Obstructive pulmonary function defects were noted in approximately 50%. Neither age nor cigarette smoking served to explain the findings. For those under age 40, obstructive findings were predominantly among cigarette smokers, as expected. After that age, however, the prevalence of changes was very much the same among smokers and nonsmokers. Of course, age correlated strongly with duration of employment. These two factors were analysed separately and it was found that the changes were generally among smokers with less than 20 years from onset of exposure, but that thereafter they were present in both smokers and nonsmokers. Radiographic changes were less common. Overall, 13.3% of 985 chest films showed linear, reticular or nodular changes characterized as 1/0 or 1/1 in the ILO U/C Classification. Dyspnœa was uncommon and signs or symptoms of chronic bronchitis were not striking (Miller *et al.* 1975, Miller 1975).

The pathogenesis of these abnormalities was not clear. It was not known, for example, whether they reflected another biological change associated with exposure to vinyl chloride monomer, or another factor. Mr A W Barnes had noted that manufactured PVC might currently contain 5 parts/10^6 of retained vinyl chloride monomer, as well as other agents added in the polymerization process. Inhalation of such PVC particles might be associated with adverse effect. Frongia and his colleagues (1974) had reported significant histopathological changes in the lungs of guinea-pigs exposed to PVC powder in a PVC plant. In the polymerization facilities investigated by Professor Selikoff, there had usually been opportunity for PVC dust exposure as well as vinyl chloride exposure, either by a period of work with the polymer during the employment span and/or as the result of incomplete separation of the various parts of the production process. PVC dust was often to be found in several parts of the plants.

It would seem of interest to study further the influence of vinyl chloride and PVC in the experimental animal, as well as the pulmonary status of workers producing vinyl chloride monomer but not exposed to PVC during or after the polymerization process.

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Review of Animal Studies

Since vinyl chloride is a gas at normal temperature and pressure, inhalation is the important route of exposure in industry, and most animal studies have used this method of dosing. Many experimental studies have demonstrated the very low acute toxicity of the compound. The acute inhalation toxicity was studied by Mastromatteo *et al.* (1960), who found that the lethal concentration for mice, rats and guinea-pigs exposed for 30 minutes was between 200 and 300 000 parts/10^6. In long-term studies few toxic effects were reported, though Torkelson *et al.* (1961) found that inhalation of vinyl chloride resulted in minimal microscopic changes in the liver and kidneys of several species of experimental animals exposed seven hours a day to 500–200 parts/10^6 for six-month periods. No significant changes were found in any species exposed to 50 parts/10^6 for six months.

In 1971, however, Viola *et al.* reported that while attempting to produce acro-osteolysis in rats, they had found tumours of the ceruminous glands, lungs and bones in animals exposed for 4 hours a day, 5 days a week, for 12 months to 30 000 parts/10^6 of vinyl chloride. Viola's findings, which are the earliest to be published describing the oncogenic effect of vinyl chloride, caused considerable concern throughout the world and led to further epidemiological and animal studies, many of which are still incomplete. The most complete series of animal studies available to us are those conducted by Maltoni and his coworkers (Maltoni 1973, Maltoni & Lefemine 1974). In these experiments groups of rats were exposed to vinyl chloride vapour concentrations ranging from 10 000 to 50 parts/10^6 for 4 hours a day, 5 days a week, for 12 months. The animals were then maintained for the rest of their lives unless they became ill. Tumours of the ceruminous glands, angiosarcomata of liver and other organs, nephroblastomata and a variety of other tumours were found in animals exposed to vinyl chloride. In animals exposed to 50, 250 and 500 parts/10^6 the logarithms of the numbers of animals having angiosarcomata and the total tumour-bearing animals are linearly related to the dose of vinyl chloride, but in animals exposed to higher concentrations, this relationship is not found. Tumours have also been found in mice and hamsters by Maltoni and by Keplinger *et al.* (1975), who reported the findings of angiosarcomata and lung adenomata in mice exposed